Minutes

Agricultural Biotechnology Research Advisory Committee

March 22-23, 1989

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U.S. DEPARTMENT OF AGRICULTURE

AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE

MINUTES OF MEETING

March 22-23, 1989

CALL TO ORDER AND APPROVAL OF AGENDA AND MINUTES

Dr. Bennie Osburn, Chair, convened the fifth meeting of the Agricultural Biotechnology Research Advisory Committee (ABRAC) on March 22, 1989 in Room 104-A, of the U.S. Department of Agriculture (USDA) Administration Building, 14th & Independence Avenue S.W., Washington, D.C. The meeting was open to the public.

Members present included:

Bennie I. Osburn, Chairman, University of California, Davis, CA;
George C. Hill, Meharry Medical College, Nashville, TN;
Richard L. Witter, USDA/ARS, East Lansing, MI;
Anne K. Hollander, The Conservation Foundation, Washington, D.C.;
Edward Korwek, Hogan and Hartson, Washington, D.C.;
Fred Gould, North Carolina State University, Raleigh, NC;
A. Ann Sorenson, American Farm Bureau Federation, Park Ridge, IL;
Ariel Hollinshead, George Washington University, Washington, D.C.;
Rodney Bothast, Vice-Chairman, USDA/ARS, Peoria, IL;
Sue A. Tolin, VPI and State University, Blacksburg, VA;
Frank W. Whitmore, Ohio State University, Wooster, OH;
Nicholas M. Frey, Pioneer Hi-Bred International, Des Moines, IA;
John D. Kemp, New Mexico State University, Las Cruces, NM;
Alvin L. Young, Executive Secretary, USDA Office of Agricultural Biotechnology, Washington, D.C.

Alternates in attendance included:

Anne K. Vidaver, University of Nebraska, Lincoln, NE;

The roster of the Committee members present is included as Appendix A.

USDA Office of Agricultural Biotechnology (OAB) staff present included: Daniel Jones, Marti Asner, Maryln Cordle, Phillip O'Berry, Bert Wenner, Martha Steinbock, Eva Russnak, Gary Weber, Elsie Brown and Barry Stone.

Others present for all or part of the meeting included:

Jane Rissler, National Wildlife Federation;
Robert J. Crawford, National Institutes of Health;
Rex Dunham, Auburn University;
H. Graham Purchase, Mississippi State University;
John Reilly, Economic Research Service;
Luther S. Williams, National Institutes of Health;
Beth Anderson, Environmental Protection Agency;
Althaea Langston, Animal and Plant Health Inspection Service;

Susan Ely, ICI Seeds;
Jeffrey Fox, Biotechnology Magazine;
John J. Cohrssen, Council on Environmental Quality;
Bob Frederick, Environmental Protection Agency;
Rudy Wodzinski, American Society for Microbiology;
Alan Goldhammer, Industrial Biotechnology Association;
Charles Peng, CLNDA;
Charles J. Eby, Hill and Knowlton;
Christina Good, Environmental Protection Agency;
Milton Freifeld, Environmental Protection Agency;
Joyce Reidietc, Environmental Protection Agency;
Lee Dexter, Agricultural Research Service;
George Anthan, Des Moines Register;
Richard Parry, Agricultural Research Service;
Michael Shaw, The CEMES Group;
Laurie Leach, The Animal Health Institute;
John McClelland, Economic Research Service;
Doreen Stabinsky, University of California, Davis;
T. T. Chen, University of Maryland;
David Morrison, Washington Aquafarm Letter;
Judith Weis, National Science Foundation;
Joel Schor, Economic Research Service;
Wesley Johnson, Food Safety and Inspection Service;
Mark Crawford, Science Magazine;
Margaret Mellon, National Wildlife Federation;
Joy Bates, Pioneer/Fleishman Hillard;
John Keegan, Theseus Research;
Jan Harsch, USDA AgriData News Service.
David MacKenzie, Cooperative State Research Service

Dr. Osburn called the meeting to order at 9:15 a.m. He noted that three voting alternatives were in attendance, George Hill replacing Harold Hafs, Richard Witter replacing John Gorham, and Ariel Hollinshead replacing Linda Phaire-Washington. Anne Vidaver was also attending as a non-voting alternate.

Dr. Osburn announced that Dr. Alvin Young, Executive Secretary, had accepted the permanent position as Director of OAB and was retiring from the U.S. Air Force. Dr. Osburn expressed pleasure that Dr. Young would be continuing in his role as Executive Secretary of ABRAC.

Dr. Osburn noted several changes in the preliminary agenda. He announced the Auburn proposal on transgenic carp would be discussed at 9:00 a.m. on Thursday, March 23.

Dr. Osburn noted that the Animal and Plant Health Inspection Service (APHIS) had prepared an Environmental Assessment (EA) on the testing of an rDNA rabies vaccine, issuing a Finding Of No Significant Impact (FONSI). As Chairman of ABRAC, he had received a copy of the proposal for review and a request that the proposal be distributed to the Committee for comment. He reported that the EA would be discussed on March 30, 1989 at a public hearing called by APHIS and that ABRAC members were encouraged to attend.

Dr. Young clarified for the record that OAB did not turn down an APHIS request to put the rabies vaccine proposal on the ABRAC agenda, and that it was an APHIS decision to go forward without formal ABRAC review.

Dr. Daniel Jones noted that OAB would like to add a discussion of conflict-of-interest to the agenda. He distributed a form based on one used by the National Institutes of Health (NIH) and asked committee members to comment on it later in the afternoon.

The agenda was accepted with these modifications and clarifications.

Dr. Osburn called for approval on the minutes of the January 22-23, 1989 ABRAC meeting. Dr. Korwek asked that the last sentence of the last paragraph of page 4 continuing into page 5 be deleted, because he had not made this statement. Ms. Hollander asked that the minutes be amended on page 11 to include the full text of the additions and clarifications that the Committee had added to Dr. Kemp's motion regarding Texas A&M confinement procedures. She also requested that on page 12, paragraph 5, that it be mentioned, that although the Committee had voted not to adopt the motion she made regarding changes in Section V of the Guidelines for Research Outside the Laboratory Involving Biotechnology (hereafter referred to as the Guidelines), they had recommended that the sense of her suggested changes be incorporated. Dr. Hollinshead said she was submitting amendments to Appendix J for the record. Dr. Tolin commented that Appendix M should be labeled as a product of the appropriate subgroup, and that the scope of her motion regarding Appendix M in the next to last paragraph of page 12 needed to be more fully recorded. With these amendments the Minutes were adopted unanimously.

THE USDA GUIDELINES FOR RESEARCH OUTSIDE THE LABORATORY INVOLVING BIOTECHNOLOGY

Dr. Osburn opened the discussion by commending the ABRAC members, Ms. Cordle and Mr. Stern for their efforts in developing the Guidelines to this point. Dr. Young added that the OAB appreciated that so many substantive comments had been received from ABRAC members. He explained the copies of the draft Guidelines had been sent to the White House Office of Science and Technology Policy (OSTP), the Council on Environmental Quality (CEQ), the Environmental Protection Agency (EPA), the National Science Foundation (NSF), and other outside bodies, not for official comment, but to keep them informed of progress. Official comments had been solicited from USDA agencies. Dr. Young also noted that the remaining transition period (of approximately 30 days) was a window of opportunity to prepare the Guidelines for submission to the Federal Register for public comment prior to the new Assistant Secretary for Science and Education taking office.

Ms. Maryln Cordle gave a slide presentation documenting the general outline of the Guidelines to date. She noted the history of the process of developing the Guidelines, and the fundamental principle upon which they have been developed -- that the safety of the modified organisms should be assessed relative to the safety of the unmodified organism. Further, she described the step-wise process of the Guidelines, beginning with assigning the unmodified organism a safety category, categorizing the type of modification, arriving at

a safety category for the modified organism, designing the appropriate level of confinement, and finally arriving at the appropriate level of review.

Ms. Cordle then summarized comments received from various reviewers. Two outside reviewers, Dr. Robert Rabin of the Center for Space and Advanced Technology, and Mr. John Cohrssen, CEQ, had made similar comments on two points:

1) that a list of information required to be submitted by the Principal Investigator (PI) for ABRAC review should be added to the Guidelines; and

2) that more detailed examples should be added about the various types of confinement.

Dr. Rabin also commented that the Guidelines should make it very clear that the level of oversight is based on the phenotypic traits of the modified organism, not the techniques used to make the modification. Furthermore, he suggested that the preamble should take a forward view, indicating that in the future various classes of experiments might be exempted. He concluded that the Guidelines should treat synthetic DNA in a manner consistent with the NIH Guidelines. Dr. Rabin and Dr. Cohrssen both believed the Guidelines were quite good, and near the stage of development necessary for publication.

Ms. Cordle then summarized the official comments from USDA agencies. The Forest Service (FS) commented that the Guidelines were realistic and operative. They suggested that a flow chart be added to the table on level of review, to make it clear that the PI must go through Institutional Biosafety Committee (IBC) procedures before coming to ABRAC.

The Cooperative State Research Service (CSRS) commented that the Guidelines were relatively clear and had benefited from ample input from the scientific community. CSRS recommended that cross species cell fusion and embryo rescue be excluded from the purview of the Guidelines. CSRS also suggested that the preamble should note that the ABRAC may elect to exempt certain classes of experiments in the future.

The Food Safety and Inspection Service (FSIS) also advocated changes in the Guidelines. FSIS believe the scope of the Guidelines is problematic. In their view, this problem could be corrected if the Guidelines were widened to include all agricultural research, not just biotechnology. FSIS also questioned why there were five safety categories for modified organisms, stating that three would be preferable.

APHIS comments were the most critical. They stated that a great many problems remained with the Guidelines including lack of specificity, lack of uniformity of review, slanting toward plants and animals, use of too many acronyms, technical incompleteness (a list of organisms is missing), and that the criteria for evaluation are unclear. Specifically, APHIS called for amending the way the change from unmodified to modified organism is evaluated, stating that the current procedure is not scientifically defensible. APHIS commented that the scope of the Guidelines should be modified, particular with regard to

synthetic DNA and non-directed mutagenesis. APHIS also stated that the Guidelines do not make clear the regulatory role, and thus inadvertently circumvent the regulatory statutes of the U.S. Government. They suggested adding a step for category three and four organisms which would require APHIS or EPA review. Furthermore, APHIS suggested that the stringency for category one or two organisms be increased stating that there seemed to be a conceptual difference between the APHIS approach and the approach taken by the Guidelines, i.e., APHIS takes the position that no escape of modified organisms should take place, while the Guidelines weigh the possibility of adverse effects from a possible escape.

Dr. Osburn thanked all those who had submitted comments and Ms. Cordle for her presentation. He asked that discussion of the Guidelines follow the OAB staff paper outlining the issues to be resolved (Appendix B). However before this, he asked the Committee to consider the two central issues flagged by outside reviewers:

(1) Should the Guidelines outline the information required to be presented by the PI (as outlined on page 8 of the Handbook, Agricultural Biotechnology: Introduction to Field Testing, henceforth referred to as the Handbook) on proposals for ABRAC review?

Dr. Young stated that OAB favored inclusion of this type of outline in the Guidelines, adding that it was the position of OAB that the Guidelines should stand alone, as a self-contained document.

Dr. Korwek asked Dr. MacKenzie why this information originally was included in the Handbook and not in the Guidelines? Dr. MacKenzie replied that if it were included in the Handbook, it could be changed without going to the Federal Register for public comment.

Dr. Tolin stated she was against including the material on page 8 of the Handbook in the Guidelines, based on NIH precedent and because it was too detailed. Drs. Hill, Bothast and Kemp agreed that the information could be presented as an appendix to the Guidelines. Dr. Tolin agreed with this approach, but she noted that the outline needed to be revised based on the current section of the Guidelines dealing with confinement.

Dr. Hollinshead suggested that a form be developed for the PI, rather than the proposed outline. Dr. Frey concurred with this suggestion. Dr. Young explained that a form requires Office of Management and Budget (OMB) approval, and that this would hold up publication of the Guidelines. Ms. Hollander and Dr. MacKenzie stated they were not in favor of a form because the PI needed to have some latitude in deciding how information should be submitted.

Dr. Hill moved that an abstracted version of the material presented in the outline on page 8 of the Handbook be included in the Guidelines. The motion was seconded. Dr. Witter clarified that this motion would include the first paragraph on page 8.

Dr. Tolin offered an amendment to the motion, specifying that requests for the following types of information should be added to the outline: A) assignment of the unmodified organism to a safety category; B) basis for selection of safety category of modified organism and, C) information on the confinement protocol selected by the PI. The amendment was seconded. It was passed, seven in favor, four against and 2 abstaining.

The motion as amended was also passed, 9 in favor, 2 opposed and 2 abstaining.

Dr. Osburn asked the Committee to consider the following question.

(2) Should examples of confinement procedures be given in the Guidelines?

Dr. Frey moved that no examples on confinement be included. The motion was seconded. It passed 12 in favor, 1 opposed and 1 abstaining.

Ms. Cordle thanked the ABRAC for their comments and assistance. Referring to the OAB staff paper on issues for discussion (Appendix B), she asked the Committee to consider Section V of the Guidelines dealing with the safety category of the modified organism, and determine if this section conveys adequate information on the evaluation factors used to determine the safety category?

Dr. Frey suggested that the sentence, "additional characteristics of the organism such as, host range, disease resistance, and fitness in the environment should also be considered to determine safety category," be deleted. Dr. Purchase suggested that these points be included in points 1) and 2) earlier in the paragraph.

Dr. Korwek disagreed, saying that incorporating these points elsewhere would not clarify them. Dr. Witter suggested the sentence be rewritten to include the concept that these points are a subset of the ability to disseminate and survive.

Dr. Hollinshead moved that this sentence be amended to read "additional characteristics may also be considered to determine Safety Category." Dr. Tolin offered an amendment that in addition to this change, that "interaction with" be inserted in the 6th line of the paragraph, between "its" and "environment" and that the next sentence be amended to read, "this determination should include, but not be limited to the study of 1) and 2)." Dr. Hollinshead did not accept the amendment, preferring the original motion.

Ms. Cordle stated that Dr. Rabin had suggested that the Ecological Society of America's recommendations be referred to in this section. Dr. Hollander stated that this could be added in a footnote. Dr. Vidaver agreed, but suggested that the footnote should also reference the rDNA Bulletin's "Points to Consider on Microorganisms."

The question was called on the original motion including the footnote. It was passed, 12 in favor and 1 abstaining.

Dr. Gould commented that he had problems in working insects into the safety categories. Dr. Vidaver suggested that in point 2) "persist in the" should be deleted and "adversely effects" be substituted, to allow for the use of beneficial insects as biological control agents.

Dr. Tolin moved that the changes she had suggested in the above amendment be made. The motion was seconded. It was passed, 12 in favor and 1 abstaining.

Dr. Korwek brought up the issue of benefits of the release in the environment. He commented that the Guidelines speak to the potential risks involved with release, but do not speak to benefits. He advised that, legally, it was necessary to weigh benefits verses risks. He suggested that a discussion of benefits, broadly interpreted, be included in the preamble.

Dr. Kemp suggested that the charge of ABRAC might not include an explicit assessment of potential benefits. Dr. Sorensen pointed out, that on a practical level, such as in the discussion of the brucellosis proposal at the last meeting it was impossible to avoid considering benefits. She added that she believes this concept is already inherent in the Guidelines. Dr. Kemp asked Dr. Korwek if he thought only economic benefits should be considered or other benefits such as public health? Dr. Tolin suggested benefits might fit into Section IX of the Guidelines. Ms. Hollander said she was comfortable with leaving the concept quite vague and seeing how it worked on a case-by-case basis. However, she strongly agreed with the suggestion that benefits be mentioned in the preamble.

Dr. Purchase noted that the phrase "adverse effects" was used to define "adverse effects," thus making the logic of this section circular. Dr. Osburn suggested that each Committee member who had been requested to give examples of each category of unmodified organisms briefly present their submissions (for submissions of examples of higher plants, microorganisms, trees, animals, and insects, see Appendix C)

Dr. Kemp said he had been asked to categorize higher plants. Working with Dr. Henry Shands, ARS, National Program Staff, he had arbitrarily divided plants into three categories: 1) crops; 2) weeds and 3) other plants. These groups were in turn divided into safety categories 1-5. He explained that most crop plants which are domesticated are classified in safety category 1). Crops which may intercross with a wild or weedy relative are generally classified in safety category 2). He classified weeds which States control in category 4) and weeds which are listed in the Code of Federal Regulations as noxious weeds in category 5).

Dr. Bothast reported that he had asked a group of colleagues to help him classify 40 microorganisms. Only two of the forty were placed in the same category by the entire group. He added that it demonstrated how difficult it was to classify organisms since the five categories really represented a continuum. He also noted that classifying microorganisms is especially difficult because different strains had to be treated differently.

Ms. Hollander asked if Dr. Bothast's colleagues had classified the microorganisms in widely varying safety categories. Dr. Bothast replied that

they had not. Ms. Hollander then stated that, if the safety categories assigned only differed by one, then this issue could be addressed in the Guidelines by instructing the PI, when it doubt, to make the conservative assumption.

Dr. Osburn stated that classifying microorganisms was indeed difficult and that Dr. Bothast's submission gave the group something to start with. Dr. Tolin agreed, saying that decisions should be strain specific, and noting that the ABRAC will gradually classify organisms as cases are represented.

Dr. Wodzinski, of the American Society for Microbiology requested that bacterial phages also be classified.

Dr. Whitmore reported on his effort to categorize tree species. He said that temperate trees are generally safe because they don't spread rapidly and he therefore recommended placing all North American species in safety category 1. He said some tropical species might fall in category 2, but no tree species should be classified in categories 4 or 5.

Dr. Hollinshead asked how sumac should be categorized? Dr. Whitmore replied he believed it should be put in category 4.

Dr. Witter explained he had a problem with the scope of the assignment on animals because he was not sure whether or not to categorize animal pathogens. He explained that he had used the Guidelines to make choices and recommended placing most large animals in category 1.

Dr. Gould reported that no insects fall in category 1, with the domesticated silkworm as a possible exception. As an example of why most insects would fall in categories 2 or higher, Dr. Gould cited Heliothis, which can travel up to 500 miles in a single generation. He said there were efforts underway to transform this species by inserting a marker gene that could allow them to be tracked. Dr. Gould also reported that his efforts to classify insects had led him to believe that the stability of adverse effects should be considered, as well as the fact that many insect pests were already widespread in the environment. Dr. Gould noted that the pragmatic approach taken by Dr. Witter is very useful.

Dr. Hollinshead said that insects had to be treated with extreme caution because of the possibility that they could serve as a vector for toxins or could be used in germ warfare.

Dr. Osburn left the meeting for a previous commitment. Dr. Bothast, acting as Chairman in place of Dr. Osburn, asked for general comments on the examples cited above. Dr. Frey stated that all plants, microbes, and animals of commerce should be in category 1 because if they are openly traded they are generally recognized as compatible with the environment (GRACE). Dr. Gould commented that this would be possible if their were two types of GRACE organisms i.e., 1) an organism such as corn which is environment-independent and cannot cross with other species 2) organisms like insects which are environment-dependent.

Dr. Bothast asked how extensive the lists of examples should be. Dr. Kemp proposed that it might be helpful to simplify the process by only having three categories of unmodified organisms, but retaining five categories for modified organisms. He said he would be more comfortable giving no examples and letting the PI decide based on the general information offered in the Guidelines.

Dr. Korwek noted that the Committee had differing views on what should be in each category. He stated it would take a long time to sort this out.

Dr. Witter noted that the possible adverse effects on natural ecosystems was the most difficult issue being addressed. He questioned whether the fact that an organism has the ability to survive and replicate makes it incompatible with a wild ecosystem? Dr. Tolin replied that specific environments need to be considered. She said ABRAC should stick with five categories. Dr. Whitmore cautioned about assigning organisms to category 3 because this may unnecessarily constrain research.

Dr. Bothast asked OAB to consider the views given and add examples to the Guidelines. He asked that Committee members contact OAB if they had strong views on this issue. Dr. Vidaver asked that it be made clear that the examples given are for the United States.
Dr. Bothast then asked for comments on Section VI, which deals with the types of modifications. Ms. Cordle asked that the Committee first concentrate its efforts in determining if the revisions made by OAB to this section were technically correct.

Dr. Vidaver requested that some of the material in the preamble in Appendix M of the January minutes which was deleted from the Guidelines, be put back in. She agreed to discuss the material that had been deleted with Ms. Cordle.

Dr. Vidaver also asked that the language be softened a bit, stating that it was not scientifically defensible to state things in absolute terms, and that phrases such as "are likely to" or "are intended to " would be preferable. Ms. Hollander commented that if the material were added back, it should continue to be made clear that conclusions are to be verified in the laboratory before experiments go to the field. Dr. Vidaver responded that deleting the material in question did not enhance the Guidelines' clarity on this point. Drs. Tolin and Frey noted that there seems to be a consensus within the Committee that the language should be softened.

Dr. Gould offered the general suggestion that parts of the Guidelines which the ABRAC considered problematic should be flagged for public comment when the Guidelines are published in the Federal Register. Dr. Young agreed with this suggestion.

Dr. Tolin recommended that the Guidelines should retain the terms "safety," "increased safety," "decreased safety," etc., throughout rather than using "risk" at some points instead of safety. Dr. Korwek concurred, saying that consistency in terminology is important. Ms. Hollander suggested that the phrase "probability of adverse effects" could be substituted, although it is wordy. Dr. Young replied that OAB would insert the word "probability."

Dr. Korwek stated that he didn't understand the inclusion of "e.g., marker genes" in Section VI-B-1. Ms. Cordle noted that APHIS had also objected to this example, saying that marker genes might be for antibiotic resistance. Dr. Frey doubted this should have any effect on risk. Dr. Tolin suggested that "marker sequence" be substituted. Dr. Frey asked if bacteria should be mentioned.

Ms. Hollander and Dr. Korwek suggested that a few more examples be given. Dr. Bothast asked if there was consensus about the need for more examples? The Committee responded that there should be additional examples added, but it was not necessary to give examples for each type. Ms. Cordle indicated that OAB would telephone members to get additional advice on examples.

Ms. Cordle asked if there were any other types of modifications beyond additions and deletions which needed to be considered. The Committee agreed that no additional types of modifications were necessary, but it requested OAB to review the section to ensure that the terminology used is consistent.

Ms. Cordle asked the Committee to consider the Section IX, "Review and Approval of Experiments." Dr. Frey commented that ABRAC was committing itself to review too many experiments, particularly with regard to SCM-2 organisms. He also stated that it was too big a step to go from the IBC to ABRAC and that there should be an intermediate step which called for OAB notification, but not ABRAC review.
Dr. Witter commented that the way the review process was meshed with the level of confinement offered the PI an incentive to add confinement in order to avoid review.

Dr. Whitmore stated that he thought that this approach was correct. Mr. Stern commented that as more experiments are reviewed and become routine it may become clearer where to draw the line regarding level of review. He added that public comment will be critical in this area.

Dr. Frey expressed concern that the Guidelines might be erring on the side of too much oversight. Mr. Stern commented it was easier to become more lenient than to become more strict over time. Dr. Kemp said he believed ABRAC should review SCM-3 organisms at confinement level 3 and SCM-4 organisms at confinement level 4.

Dr. Tolin said that there should not be a gray area (termed N/A) on the table which describes the level of review and that "not recommended" or "laboratory" should be inserted instead. Dr. Kemp stated that contained experimentation should not be part of the Guidelines. Ms. Hollander suggested using the phrase "not recommended." Dr. Hollinshead agreed saying that the words "not recommended;" move to a higher confinement level" might be substituted. Dr. Purchase said it should be made clear that all proposals must go through the IBC before they come to ABRAC.

Dr. Young and Ms. Cordle said that these adjustments would be made by OAB, but the issue remained, is the level of review correct?

Dr. Kemp moved that SCM-2 organisms at confinement level 2 and that SCM-3 organisms at confinement level 4 be listed as "IBC approval with notification to OAB." The motion was seconded.

Dr. Langston recommended that the table should include a footnote reminding the PI that regulatory approval is still required. The Committee accepted her suggestion by consensus.

Dr. Vidaver suggested that the title be changed to say "Field Research" rather than "Research Outside the Laboratory" because contained facilities such as greenhouses are not laboratories.

Dr. Jane Rissler, National Wildlife Federation (NWF), stated that underlying principles should be discussed at this point. She said the only justification she had heard for reducing the levels of review was to reduce the ABRAC workload, and that the NWF would prefer more stringent review levels. She asked the Committee to explain its interest in reducing the levels of review required, as stated in Dr. Kemp's motion. Dr. Frey responded that the draft Guidelines did not accurately reflect earlier ABRAC recommendations and the levels of review originally described could not be justified scientifically. Dr. Young added that OAB had put the Table 2 together.

Dr. Rissler asked what the principle was behind determining review levels? Ms. Hollander replied that decisions were based on risk relative to confinement level. Ms. Hollander said that such decisions were subjective, but she wanted the record to show that it is not just a workload issue, but that scientific risk assessment is involved.

Dr. Rissler stated again that she would prefer slightly more stringent requirements to begin with. Dr. Young said that the public would comment on the desired level of review.

Dr. Frey commented that it is only experiments that fall on the boundaries between categories that raise questions. Ms. Hollander reiterated that the Guidelines should include language saying when in doubt, move to the next higher category.

Dr. Kemp raised the possibility that there may be gerrymandering with people driven to look for "good" IBCs.

Dr. Tolin noted that she supported Dr. Kemp's motion amending the table, noting that the amended table was very close to earlier hand-drawn tables submitted by an ABRAC Working Group.

The Committee voted on Dr. Kemp's motion to amend the table and it passed, 9 in favor, 3 against and no abstentions (one member was out of the room during the vote).

Ms. Cordle then asked the Committee to review the scope of the Guidelines, noting that this section of the Guidelines is based on the NIH Guidelines, but is more conservative. Dr. Tolin said that she agreed with the more conservative approach because the Guidelines covered work in the field, as

opposed to work in contained facilities, and in addition, the Guidelines were covering new techniques.

Dr. Korwek asked why the Guidelines explicitly mentioned synthetic DNA? Dr. Frey suggested that reference to synthetic should be deleted. Dr. Hollinshead said she believes the Guidelines would be simple and descriptive, and there was no need to specify types of synthetic DNA. Dr. Kemp disagreed, and asked, what about the situation when synthetic DNA differs in base sequence from natural DNA, but has the same function? He added that the sentence in question did not speak to functionality. Dr. Hill said the potential functioning of the synthesized gene is important. Dr. Whitmore stated that the key point that should be made clear in the Guidelines is that artificial methods are the same as natural methods, irrespective of what the sequence is. Dr. Tolin suggested that the sentence should read "synthetic DNA segments are considered the same as natural DNA segments ...." Ms. Cordle asked if the sentence should refer only to synthetic DNA or should it include synthetic RNA as well? By consensus the group decided to cover only DNA.

Dr. Purchase questioned the need for the phrase "stable and transmissible" in the first sentence. Dr. Sorenson agreed, saying the Guidelines should cover biotechnology research outside the laboratory which involves genetic changes in organisms. Dr. Vidaver stated that the Guidelines should cover all research on genetically modified organisms that takes place outside contained facilities. Dr. Korwek replied that the Guidelines had best stick to agriculture, since legally, it was the ABRAC's charge to deal with agriculture.

Dr. Vidaver suggested that the title of the Guidelines should be changed to say research in the field or outside contained facilities. Dr. Tolin agreed.

Ms. Cordle asked the Committee to consider an issue raised by several reviewers, i.e., what is the scientific justification for excluding embryo transfer within a species, but including cell fusion and embryo rescue? Dr. Frey said embryo transfer within species was now very common and safe, but crosses between species could involve genetic material from a pathogen. Thus, he believed the Guidelines were correct on this point and should not be changed. The majority of the Committee agreed that this was scientifically justifiable and that the Guidelines should retain the language in question.

Dr. Gould asked that it be noted for the record that he strongly disagrees. He said his experience with insects, and his reading led him to believe that crosses made by hand pollination or artificial insemination between species should also be covered by the Guidelines. He stated, that he believed there was no scientific justification for not putting these in the purview of the Guidelines and that he favors beginning with very broad oversight and then granting exemptions for such things as crop plants.

Dr. Hollinshead stated that the science in the scope section seems weak. She stated, that she was bothered by the need for differing treatment of plant, animal, and insect species with regard to crosses between species. Dr. Korwek also noted that he had problems with the section, stating that there seemed to be a lot of interweaving between concepts. He believes the section also has a

process-based flavor and he concurred with Dr. Gould's misgivings and said that it would be better to put exclusions, if there were to be exclusions in later sections.

Conflict of Interest

Dr. Bothast asked that the Committee, at this point, to consider the conflict of interest form distributed earlier by Dr. Jones, and return to discussing the Guidelines later.

Dr. Korwek requested that the form be revised. He said the form leaves too many questions unanswered, and that he could not sign in its present form.

Dr. Kemp raised questions about financial interest in mutual funds where a member has no control over decisions about investment.

Ms. Hollander said that ABRAC members needed clear criteria for conflict of interest. She urged OAB to check with EPA and other agencies to see how they were handling this issue. Two aspects that need to be addressed are: 1) what about a member who receives grant money from a company which submits a proposal and 2) can a member from a private company review proposals from competing firms? OAB agreed to check with other agencies and address these issues.

The USDA Guidelines for Research Outside the Laboratory Involving Biotechnology

Dr. Young asked the Committee to again focus on the scope of the Guidelines, stating that exclusions had to be written clearly.

Dr. Kemp suggested that in the first sentence of paragraph 5 to be changed to read, "... that occur in nature or have a good chance of occurring in nature." He suggested that the techniques listed in the remainder of the sentence be moved to an appendix that would list exemptions specific to different types of organisms. Dr. Frey responded that he generally did not favor adding appendices, but he did support the concept of occurring in nature. He said he sees this as clearly different from techniques which occur with human intervention.

Dr. Tolin suggested that the group refer back to Annex M, page 2 of the January ABRAC Minutes, where the Committee had given justification for a "manageable spectrum of changes." She said this language could be incorporated into the scope of the Guidelines. She added that "adverse effect" was not mutually exclusive of "occurring in nature," noting that bad things can happen naturally.

Ms. Cordle asked if the language proposed by Dr. Tolin is compatible with Dr. Frey's point of natural versus human intervention. Dr. Tolin said that it is. Dr. Korwek stated that he would support exemptions but he believed the phrase "occurring in nature" was difficult to get a handle on. He proposed that "domestification" or "long history of use" would be better. Dr. Kemp said that these concepts are related. Dr. Korwek agreed.

Dr. Whitmore questioned if the Committee was being careful enough to clearly exempt things that have gone on for some time e.g., classical breeding techniques. He cautioned that hydridization of forest trees had been going on for fifty years safely, but it had very little chance of occurring naturally. He said the Committee should consider these exemptions carefully.
Ms. Hollander said that she favored including techniques in the oversight of the Guidelines because these would fall into low risk categories.

Dr. Kemp suggested adding an appendix that would exempt hand pollination for plants. Dr. Gould urged caution, saying that if hybrids grow twice as fast as the parent plant, then this change impacts the ecosystem. He said he was not against broad exemptions, but hoped the Committee could arrive at these coming from another direction.

Dr. Korwek noted that, historically, giving exemptions later has been very hard to justify from a legal point of view, thus it is better to build them in up front. Dr. Kemp agreed exemptions should be included now.

Dr. Whitmore suggested changing the word "exempt" to "does not apply." He noted that the ABRAC had begun by advocating very broad oversight and was ending up there again.

Dr. Hollinshead stated that she was submitting her suggested changes to OAB for consideration.

Dr. Bothast asked if the group favored or was against appendices to the Guidelines. Dr. Tolin responded that she believed that things should be included up front without too much material, but a few examples should be left in.

Dr. Gould said the ABRAC should not exempt on the basis of a technique. Instead he recommended that techniques be associated with their contexts. Dr. Tolin said the ABRAC needed to leave some discretion in the hands of the scientists.

Dr. Korwek advocated leaving the rewriting of the scope section to OAB. He said that methods are associated with certain products and the section needs to be covered in those terms. Certain plants may be exempted but the Guidelines need to give reasons. Examples include a long history of safe use, familiarity with improved species, etc.

Ms. Hollander stated that she believed that this was giving OAB an impossible task - to write a process-based but scientifically justifiable scope section.

Dr. Korwek responded that the National Academy of Science (NAS) is looking at a new approach to this issue. He said if the Guidelines are product-based, they pull in lots of old techniques, yet process history attaches to products. Dr. Whitmore agreed, saying that because we're familiar with products we're aware of what limits there are on particular processes. Ms. Hollander said she would go along with letting OAB try, but she believed the task was difficult.

Ms. Cordle asked the Committee to consider Section VIII of the Guidelines which pertains to confinement. She asked if the Committee wished to say that "organism" was defined as "organism and its products" where relevant? The Committee agreed to this by consensus.

Ms. Cordle then asked the Committee to consider the revisions to Section VII on the safety categories for genetically modified organisms.

Dr. Witter commented that this section of the Guidelines raises problems when dealing with animals. He added, that most umodified animals will fall into categories 1 or 2. However, transgenic animals may become "exotics," with the result that the safety category of the modified organisms (SCM) may be raised more than one level.

Dr. Tolin stated that an automatic one-step increase with type three modifications is not scientifically justifiable and stated that the PI is the person who knows the organism the best. She said the IBC should raise questions if the level of change does not seem appropriate. Dr. Witter agreed, adding that this section should be amended to explain that both type 1 and type 3 modifications may result in a change of more than one level.

Ms. Cordle noted that raising the level was not problematic because this would require more confinement and increase the level of review. She added that the problem was with type 1 modifications that lowered the SCM more than one level. Ms. Cordle recommended changing the language so that if the level changed by more than one level, the proposal automatically would come to ABRAC.

Ms. Cordle then asked the Committee to focus on Table I on page 10, noting that it will be modified.

Drs. Witter and Whitmore said the table should be retained, but the right hand column amended to say SCM 2-5 with explanatory notes. Dr. Gould said he believed the table is redundant because Table II makes it clear that if you go up more than one level you must submit the proposal to ABRAC.

Mr. Stern asked the Committee to consider the concept of voluntary compliance addressed in Section II of the Guidelines on applicability. He said, three areas needed to be addressed. 1) institutions not supported by USDA, 2) research approved by another Federal agency and, 3) research not within the scope of the Guidelines.

Dr. Frey said he was not pleased with the sentence in parentheses, "(Institutions are, nevertheless, encouraged to comply with the biosafety practices and procedures of these Guidelines even though the research is approved by another Federal agency)." He said this made it seem as if the Guidelines were implying that you could get regulatory approval without assuring safety, and they should not imply this. Ms. Hollander suggested substituting "principles" for "policies and procedures."

Dr. Korwek noted that the section is difficult, but in general, he is happy with it. However, he did agree that the sentence in question sounded a little pejorative. Dr. Korwek also said that the last two paragraphs were philosophical in tone and perhaps, they should be moved up to the section on purpose. Dr. Hill agreed with both points made by Dr. Korwek, stating that he believed the parenthetical sentence in question should be omitted, and the second and third paragraphs should be moved up to the Purpose section.

A straw vote indicated the Committee favored deleting the parenthetical sentence in question.

Mr. Stern then asked the Committee to consider the last sentence in the introductory paragraph of Section IV on the scope of the oversight of the Guidelines. Dr. Witter said he understood the difficulty with this sentence. He added that ABRAC should not side-step this issue, and that he had the sense that ABRAC would prefer experiments not covered by the Guidelines to be submitted voluntarily to the ABRAC.

Dr. Young asked the Committee to carefully consider this point. He pointed out that OAB is in a difficult position, given the severe problems that APHIS has with the Guidelines as currently drafted. He said Dr. Bentley has the option to go ahead with the Guidelines without APHIS' approval, and that APHIS had taken this approach with its bioengineered plant pest regulations. However, he believed that ABRAC should try to reach a compromise with APHIS.

Dr. Korwek stated that he had substantial disagreements with some of APHIS' comments. He said that he was surprised with the contents of their comments since earlier conversations with Dr. Langston had led him to believe that some of these issues had been resolved.

Dr. Bothast suggested that the Committee members carefully consider APHIS' comments during the evening and that they be discussed in the next day's session.

Mr. Stern then asked that the Committee review the provisions for IBC's in Section X on page 16. He said that the requirement of two outside members would act as a safeguard that the public interest was being served. He also noted that such safeguards had to be balanced with the need not to overload the IBC's with requirements since many IBCs were constrained by the size of the institution.

Drs. Vidaver and Hill asked if the provisions are consistent with the IBC's formed under the NIH Guidelines. Mr. Stern replied that it depends on how individual IBC's are formulated. Although the NIH Guidelines do not call for agricultural experts, many IBC's have already added them. He noted one other difference was that the Guidelines call for six members and NIH guidelines call for five.

Ms. Hollander said that although consistency with NIH was desirable in some instances, in other areas it might not be. She reported that a Government Accounting Office (GAO) report indicates that not all IBCs work well. She

also said she believes all IBCs should be required to have an ecologist as a member.

Ms. Cordle noted that ABRAC had decided earlier not to list explicit disciplinary titles required, because titles were often misleading in contemporary academia. Ms. Hollander agreed it might be possible to go with descriptions of expertise needed rather than titles. Dr. Wodzinski agreed that this approach was better.

Dr. Lowell Frobish, Auburn University, asked why ABRAC believed it to be necessary to dictate to institutions how to put together an IBC? He said it made it seem as if institutions were trying to hide something. Dr. Bothast said this point was well taken.

Dr. Rissler said that comments submitted by NWF on the earlier draft still apply. Furthermore, it was NWF's position that the Guidelines did not make enough of a commitment to public disclosure and public participation. Continuing, she said she was not convinced that the need to ensure the public interest is being met by including two non-affiliated members on the IBC's. She recommended including a provision which would require an IBC to hold a public meeting if 10 people petitioned them to do so. She also said the Confidential Business Information (CBI) provision should make it clear that only sections, not an entire proposal, can be withheld from the public for this purpose.

Dr. Bothast suggested that the Committee adjourn for the evening and consider these issues after the Auburn proposal is discussed in the morning.

Auburn Proposal on Transgenic Carp

Dr. Osburn asked the Committee to consider the Auburn University request to conduct Experiments to Evaluate Common Carp Containing the RSV Rainbow Trout Growth Hormone Gene (rtGHg) for Inheritance, Expression, and the Biological effects of rtGHg in Experimental Ponds (henceforth referred to as the transgenic carp proposal), addressing the biosafety issues involved and the way the proposal fits into the Guidelines. He explained that Auburn University was voluntarily submitting the proposal for ABRAC review.

Dr. Jones presented the history of the transgenic carp proposal. He said that CSRS had received the original request for review on December 8, 1986, and had passed the request to OAB. He noted that the PI had sought and received IBC approval of the proposal in October 1986 but at that time there was no ABRAC and no draft Guidelines. Dr. Jones noted that the original proposal was considerably broader than the transgenic carp proposal now before the Committee, in that it covered several species and several genes. He said that Auburn and OAB recognized that an Environmental Assessment (EA) would be necessary. OAB had sent the proposal to eight outside reviewers including experts on freshwater aquaculture and had sent two teams on site visits to Auburn University. Following the second site visit, the PI sharply narrowed the focus of the proposal so that it now deals with a single species (common carp) and a single gene (trout growth hormone). Dr. Jones also reported that OAB had held a meeting the week of March 13, 1989 with other interested

Government agencies including, EPA, FDA, FSIS, APHIS, and the Fish and Wildlife Service. They raised some concerns and asked that, if the ABRAC recommends approval of the proposal on transgenic carp, that an EA be published in the Federal Register.

Dr. Rex Dunham, the PI for the experiments on transgenic carp gave a slide presentation on the proposal. Dr. Dunham pointed out that the first fish gene transfer was reported in China in 1965. The first such transfer in the United States was reported by Auburn in 1985. Since then 12 or 13 laboratories around the world have reported a positive biological impact, i.e., increased growth in the fish from gene transfer experiments.

Dr. Dunham stated that one goal of the experiment was to demonstrate, in a pond environment, what had already been achieved in the laboratory i.e., that the rtGHg could be transferred, expressed, and result in a biological effect. Another goal is to demonstrate that these results can be achieved in a warm water fish and that the biological effect will be positive, i.e., increased growth. Such results might eventually be helpful in working with channel catfish.

Dr. Dunham reported that the experiment was being conducted in cooperation with Dr. Thomas Chen and Dr. Dennis Powers of the University of Maryland, Center for Marine Biology and Johns Hopkins University, respectively. The gene construct was provided by Drs. Chen and Powers. Purified DNA is shipped to Auburn from their laboratory and then microinjected into embryos. The fish are cultured at Auburn, and then DNA isolated from tissue samples is shipped back to Drs. Chen and Powers for final analysis.

Dr. Dunham stated that the carp have been transformed using a pRSV-2 based plasmid containing a cDNA sequence. The recombinant clone was linearized prior to microinjection.

Dr. Dunham reported that the experiment was being carried out using an Israeli strain of common carp, called mirrored carp, which is not fully scaled. The mirrored carp is less streamlined than other strains of common carp and has a high dorsal projection. In some cases the experiment also uses color mutants. He said these traits are carried in two loci, homozygous recessive and homozygous dominant, and that they breed true, with all progeny being partially scaled. Thus the experimental carp are readily identifiable even without laboratory analysis.

Dr. Dunham then described the proposed experiment. He stated that he and his fellow researchers intended to control reproduction through artificially timed and induced ovulation. Fertilization would occur in petri dishes, and then 10^6 - 10^8 copies of the gene would be microinjected into embryos at the 2 or 4 cell stage. He reported that laboratory blot analysis data indicates that 1-5 copies are integrated and that probes confirm that the gene is integrated. He added that multiple copies are inserted at possible multiple sites and that in the laboratory, they had achieved expression. This had been demonstrated by radioimmunoassay, which showed that the level of protein expressed varies between 8 and 89 ng/mg P. The rate of expression is not correlated with the amount of DNA incorporated.

Dr. Dunham reported that, in the laboratory, transformed carp are growing 20% faster than controls, and are 40-50% larger than controls. He said that subjective observations of behavior in the tank noted no differences between the transformed carp and the controls. The fish were equally easy to catch. Furthermore, there was no increase in deformities in the transformed fish.

Dr. Dunham said that the proposed experiments would involve rearing transgenic brood fish in outdoor, experimental ponds. The transgenic fish would be spawned indoors and the embryos hatched and initially raised in the laboratory. The transgenic progeny would then be raised and evaluated in the outdoor experimental ponds and their performance would be measured. Dr. Dunham added that they had data from laboratory experiments, but needed to know what would happen in ponds. He said that it was very difficult to mature fish indoors, and that working outdoors greatly increased the chances of success in maturing fish. Indoors there is a very high mortality rate both for transgenic and control fish. Only six transgenic fish remain - 3 males and 3 females. Beyond the advantages in rearing fish, working in experimental ponds would allow evaluation of environmental-genotype interactions.

Dr. Dunham then noted the measurements that would be taken in ponds: the growth rate of individuals at various stages of development; the reaction to stress, including survival at all stages for the first two years; biosafety monitoring; relative ability to harvest; 7 or 8 detailed body composition analyses, the rate of inheritance of the introduced gene; and sexual development including the counts of eggs and sperm and age to maturity in about 40 or 50 of the second generation fish.

Dr. Dunham then described the confinement that would be used for the proposed experiments. Physical confinement would include sealed clay ponds with levees, bird netting and screens (25 micron mesh) for incoming and outgoing water. The experiment will be conducted under static conditions and thus, there will be no intentional flow of water through the ponds. The ponds are above the 50 year flood plain and will not be filled within 5 inches of the top to allow for rain. Ponds will be fenced with a chain link fence (8 feet high) and topped with two strands of barbed wire to keep out human and animal predators. Scale would also be used to help ensure biosafety because only 10 small ponds of .10 acre each totaling 1 acre would be used. Dr. Dunham stated this is considerably less acreage than is normally used in fish experimentation. The number of fish will also be monitored, and kept at no more than 300 fish per pond or 3,000 fish per acre.

Dr. Dunham then described the biological confinement procedures that would be used. Brood fish will be spawned indoors and the sexes will be separated during breeding. Fish gametes are viable for only one minute or so, and fertilized eggs of carp are adhesive, making escape improbable.

Upon termination of the experiment chemical barriers will be used to ensure safety. Ponds will be drained and dried and any of the pond bottom that has water remaining will be poisoned with Rotenone to ensure that all fish have been eliminated.

In terms of security, Dr. Dunham reported that the area will be locked, posted and lighted. Personnel associated with the project will be working in the area each day and will monitor it closely. Additionally, personnel and university police will make four patrols at night. A log will be maintained of all security checks.

Dr. Dunham reported that provisions had been made to monitor possible escape and for emergency response. Fish would be individually heat branded when they weigh 30 grams. This, in combination with the scale and color mutations would make the fish readily recognizable. The public and Alabama Department of Conservation and Natural Resources would be informed that any carp with a brand or with lack of scales or an unusual color should be brought to the university for diagnostic tests. A reward would be offered for the capture of these experimental carp.

In answer to concerns about possible burrowing animals, Dr. Dunham said that the levees are generally too thick to allow them to enter the ponds. Only 10% of the ponds have levees narrower than 4 feet and these are flanked by adjacent ponds. He indicated that all levees will be monitored.

A climatology expert will be asked to monitor the experiments and inform the PI of impending flooding. If such an event is forecast, the fish would be removed from the ponds and the ponds would be poisoned. Any fish remaining would die within 5-10 minutes.

All the physical confinement barriers will be examined weekly and all inspections will be logged. Access to the environmental ponds will be restricted to personnel who have received training on confinement, biosafety, and emergency procedures. Personnel will be required to pass a written examination indicating a high working knowledge of these procedures.

Dr. Dunham reported that Auburn University was taking steps to ensure public awareness and involvement. These included having community members as part of the Institutional Biosafety Committee, giving lectures, issuing press releases and in communicating with local, state, national and international media about the experiments and holding consultations with industry and non-governmental representatives. Chiefs of the Fisheries Departments in eight neighboring states and two regional fish and wildlife steering committees have also been informed of the proposed experiments.

Dr. Osburn then asked the Committee for comments and questions about the proposed experimental protocol.

Dr. Thomas Chen offered to answer questions on the molecular biology of the experiment.

Dr. Hollinshead asked if the gene is registered with the American Type Culture Collection (ATCC). Dr. Chen replied that it is not a microorganism and is therefore not registered with the ATCC. Dr. Hollinshead then asked if the gene is patented. Dr. Chen replied that a patent is pending.

Dr. Kemp asked how long is the coding sequence? Dr. Chen replied that the coding sequence is a cDNA including about 970 base pairs which code for 199 amino acids. Dr. Kemp then asked how this compares to the normal growth hormone in carp? Dr. Chen replied that the normal growth hormone gene in carp has not yet been characterized in detail, but the gene is about the same size as the salmon or human growth gene. Dr. Kemp asked if the clone codes for a growth hormone that has been expressed in another organism. Dr. Chen said the cDNA has been expressed in E coli and the product has been isolated in juvenile rainbow trout. Dr. Kemp asked how widely used is the LTR promoter? Dr. Chen replied that the promoter is able to drive the expression of genes in a wide variety of cell types.

Dr. Hill asked if there are any other sequences other than the LTR promoter and the growth hormone cDNA injected? Dr. Chen said that the entire plasmid of 5.5 kb is injected.

Dr. Kemp asked if Dr. Chen was sure the entire DNA is integrated? Dr. Chen replied that, roughly 60 percent of the bacterial plasmid is integrated.

Dr. Kemp asked how much growth hormone do you normally find in the blood of a fish? Dr. Chen said in most unmodified fish it was 4 or 5 nanograms. In the transgenic fish the level of growth hormone ranges from 8 to 18 nanograms per milligram based on blood cells.

Dr. Kemp asked how much growth hormone is naturally produced in the pituitary? Dr. Chen said that he didn't know.

Dr. Osburn asked if the carp growth hormone is produced in red cells. Dr. Chen said no.

Dr. Gould asked what would be the advantages of using other promoters referred to by Dr. Chen? Dr. Chen said the main advantages of the other promoters are tissue specific expression and estrogen-regulated expression.

Dr. Kemp asked if Dr. Chen had performed a northern blot analysis to survey tissue expression of the LTR in the transgenic fish?. Dr. Chen replied not yet.

Dr. Hill ask why the level of expression is not merely related to the copy number? Dr. Chen replied that this is due to the site of integration of the gene. The gene may be integrated at places in the genome where expression cannot occur.

Dr. Hollinshead said that in her experience with animals it was necessary to have randomized controls and one must ensure that each animal is getting the same amount of feed. She asked how they were feeding the fish to insure that individuals were receiving the same amount. Dr. Dunham replied that the fish feed as a social unit and that individuals cannot be isolated for feeding. If the number of individuals in a cage falls below a certain level, they will fight instead of behaving normally. He said that full siblings (transgenic and unmodified) will be kept together to provide controls, but it is impossible to know how much feed individuals are eating. He said the research

team will feed the fish ad libitum and allow them to express their growth potential.

Dr. Hollinshead asked if the project includes a fish pathologist? Dr. Dunham replied they had four fish pathologists on staff.

Dr. Korwek asked why Dr. Dunham had decided on this particular scale for the experiment? He said it seemed large to him. Dr. Dunham replied from the fish science perspective, this was the smallest the experiment could be and still meet statistical requirements. He said they need to have 4-5 different matings in two units each, thus necessitating 10 different ponds. He said this number of replications of pairs is necessary to properly evaluate growth rates. He also reported that the proposal was at the low end of the stocking density needed to properly evaluate stress.

Dr. Tolin asked about the pathology of the vector. She said the proposal stated that it is a non-infectious promoter. She asked Dr. Chen to comment on this, and whether it interacts with endemic fish and whether the LTR is involved in the interaction. Dr. Chen replied that the LTR is generally accepted as not being infectious based several scientific studies. He said there is evidence that there are other viruses latent in fish, but they are not fully characterized. Dr. Dunham added that he is not aware of any herpes type virus in common carp and that he has not experienced any fish mortality caused by viral infections in the experiments thus far.

Dr. Kemp asked where the piece of DNA is integrated. Dr. Chen replied, that one can only judge that its integrated at more than one site, but cannot say where on the chromosome and that more analysis needs to be done to know precisely where.

Dr. Tolin asked about the approximately 400 base pairs which are inserted, but are not part of the coding sequence. Dr. Chen replied that they are the untranslated sequence of the messenger RNA.

Dr. Rissler asked if non-lethal integration might have effects on other traits. Dr. Chen said that if a large number of fish were surveyed it might be possible to see an increase in the rate of deformities. But Dr. Dunham added that with the small number of fish thus far, (20 fish) the transgenic fish showed no more deformities than did controls. Dr. Dunham clarified that the controls were also being microinjected with DNA.

Dr. Gould commented that Dr. Dunham had said the transgenic fish were 40-50% larger than controls. He asked how many standard deviation units larger than the norm this was. Dr. Dunham replied that it was 2-3 standard deviation units larger. Dr. Gould asked if any of the transgenic fish were smaller? Dr. Dunham repled that none were smaller.

Dr. Osburn then asked the Committee to classify the experiment using the Guidelines.

Drs. Kemp and Vidaver inquired about the viability of this strain of scaleless carp relative to the other strains of common carp. They stated this was

important to know, in order to assess the relative survivability of the unmodified organism in nature. Dr. Dunham replied that Israeli scientists have reported that the mirrored strain grows 10% slower than other genotypes and are slightly subviable.

Dr. Witter asked when the strain was imported into the United States? Dr. Dunham replied in the late 1950's or early 1960's. Dr. Witter asked if there are any restrictions on the use or dissemination of the fish by regulatory agencies? Dr. Dunham said that there had not been a deliberate release of the fish into the environment, and that only one or two fish farmers had attempted to culture them.

Dr. Sorenson asked if they reproduced normally. Dr. Dunham said they are highly fecund like other strains of carp. One female could produce 500,000 eggs.

Dr. Witter proposed that the strain of the unmodified be put in category 2. He said his proposal was based on the facts that they is no pathogenicity, toxicity, or infectivity, but they can integrate in the environment. Dr. Kemp agreed.

Ms. Hollander said that the data seemed to come from only one or two experiments, and in general the ABRAC needed to have more data before classifying experiments. Dr. Osburn replied that the ABRAC might often be faced with situations where data are limited.

Dr. Gould proposed that the modification on the carp be classified as a type 3 modification because of the increase in size of the modified organism. He said a change of size of this magnitude may have ecological consequences. Dr. Kemp stated that he was not convinced that it was a type 3 modification because he had no evidence to suggest that a larger fish was an "adverse effect." Dr. Dunham responded that general laboratory experiments indicate that growth hormones in fish affect their rate of attaining sexual maturity and that there is a relationship between age of maturity and size, however the effect on carp is still unclear.

Dr. Gould and Dr. Witter said the type 3 was the most reasonable classification because it covers effects which "are not well understood."

The consensus of the Committee was to classify the experiment as a type 3 modification.

Dr. Osburn then asked the Committee to consider the safety category of the modified organism (SCM). Dr. Kemp stated the SCM, according to the table on page 15 of the Guidelines could be 3,4,or 5. He added that if it were SCM3 the experiment could be carried out with only IBC approval. Dr. Tolin said that since the experiment was being done with physical, biological, and chemical confinement procedures, it was at least meeting the requirements for confinement level 3.

Dr. Witter questioned the proposed designation of SCM3, noting that the modification might result in raising the classification more than one step.

He said that this experiment was a good test of the Guidelines in dealing with animals.

Dr. Osburn then asked that the designated commentators give their presentations. Dr. Gould summarized his written comments which are attached as Appendix D. He said that the Committee was only considering risks, but that benefit might also be considered. He noted that this issue is related to a larger question, i.e., is the ABRAC just a biosafety committee or does it have responsibilities for evaluating other aspects of experiments? He said that his opinion was that the experiment could be modified to reduce risk of escape by containing the fry until they reached a certain minimum size.

Dr. Osburn stated that the ABRAC should stick with biosafety and that questions about the design of the experiment should be delegated to the peer review process. He said other aspects of the experiment could be considered as they relate to safety.

Dr. Witter said he had examined the transgenic carp proposal from the point-of-view of the Guidelines. He did not address scientific merit because he agreed with Dr. Osburn that it was outside the purview of the ABRAC. However, he said that he concurred with the view of the PI, that conducting the experiments outdoors was necessary because of the increased viability of the fish. Dr. Witter then addressed the LTR promoter, relating it to Avian retroviruses. He said in the domestic chickens for example, similar viruses can produce adverse effects. They may effect other genes, for example insertion near a host gene may result in the development of a lymphoid tumor. He said that he saw no evidence that this would be a problem in the experiments under discussion, but presumably there are oncogenes in fish. Presumably the fish pathologists will be monitoring the experiment for this type of effect. He also noted that another kind of adverse effect from endogenous retroviruses is that they can cause tolerance to injection from other retroviruses. This did not apply to these experiments because there is only one LTR in place. In summary, he stated that he believes these types of possible effect are not dangerous enough to preclude doing the experiments.

Dr. Witter then said his one concern with the proposal was the time frame. The experiments seemed to be somewhat open ended. The initial phase was 2 months to 1 year, and producing the next generation would take a year, but it was not clear what would happen to the fish at the end of this period.

Dr. Korwek said that he would defer to the Committee's judgement about the confinement outlined in the proposal. He said the from a legal point-of-view, it would be better to have more information about the protocol and the molecular biology. He also asked why the experiment was being conducted using carp and not catfish? He said the Committee needed to understand the rationale for the experiments. He agreed that Dr. Witter had pin-pointed a critical issue i.e., the time frame for the experiments.
Ms Hollander summarized her written comments which are attached as Appendix E. She said that from the public policy perspective, the proposal raised a number of long-term policy issues. She said that presently no Federal agency has regulatory authority for transgenic fish and this should be clarified. She recommended that USDA take the lead in organizing an interdisciplinary unit to

start working on this. She said that she had little doubt the proposed experiment would have benefits, but the benefits were not well developed in the proposal. She said that she sympathized with the PI on this point because it was a learning process for ABRAC in terms of what information to request. Another area which she believed needed more clarification was the step-wise experimental process. She said that data derived from various steps in the experiment (small scale contained a large scaled contained) should have been included in the proposal. She also said that in her opinion, fish experts should have been asked to participate in the ABRAC review process including reviewing the final proposal and attending the meeting to answer questions. Lastly, she recommended formation of a subcommittee to help evaluate these issues.

Dr. Dunham responded to the commentators that Auburn University was also involved in a learning process regarding the proposal. With regard to the length of the proposed experiments, he stated that if the experiment could go forward immediately, it would take about two years to complete. However, if it could not go forward right away, it would take about three years to complete because of the breeding cycles of the fish. He also stated that there would be scientific merit in keeping at least some of the transgenic fish alive at the end of the experiments, but a second proposal would be submitted if this were desired.

Dr. Kemp stated that the Committee could approve the experiment for a limited period of time, for example, two years, and require that the fry be a minimum size before they are released into the ponds. He also said it might be wise to decrease the number of fish held in the ponds during the winter flood season.

Dr. Osburn then opened the discussion for public comment. Dr. Rissler congratulated Auburn on their willingness to work with ABRAC on the proposal. She said that she would not repeat her written comments which are attached as Appendix F, however she did wish to emphasize the public policy issues involved. She said the NWF would prefer that the U.S. Government establish clear regulatory authority for transgenic fish, before the experiment proceeds. Furthermore, she said that, given experience with exotic fish, experimentation in the area of transgenic fish should be approached with great caution.

Dr. Rissler also observed that, in her opinion, ABRAC was basing its decision on anecdotal, rather than written data. She said the ABRAC should be enlarged to include fish biologists and fish ecologists during the review of this proposal. Lastly, she noted that it seemed that Auburn had skipped a step in the proposed protocol, i.e., raising the fish to sexual maturity indoors. She closed her statement by recommending that because this is a precedent setting proposal, and that she would recommend the following: 1) that the PI be asked to supply additional data in certain areas; 2) that an ad hoc group of experts be formed by ABRAC to evaluate the proposal and, 3) Auburn should explore alternative ways to proceed with the research.

Dr. Judith Wise, NSF, said she had been working with fish for over twenty years. She stated that, based on her work with smaller fish species, once

individuals of various sizes were put together, the faster growing fish actually secrete something into the water which inhibits the growth of the smaller fish, and thus the size disparity widens.

Dr. Vidaver asked how Auburn would measure stress? Dr. Dunham replied that it would be primarily through seeing if there was a difference in mortality between transgenic fish and unmodified fish.

Dr. Gould postulated that for large fish an experimental pond might be considered a contained facility.

Dr. Hill asked why the mortality rate was so high inside the laboratory. Dr. Dunham replied it was because of increased stress, increased incidence of disease, and related water quality problems.

Dr. Osburn offered some general observations about the proposal. He said the Secretary had decided that the proposal should go to ABRAC, despite the fact that the Guidelines were not yet complete. He said the Committee had been asked specifically to look at the biosafety aspects of the experiment. He also noted that the format for requesting information from the PI wasn't complete yet, and ABRAC had learned a great deal about what should be included in the format from the process of evaluating this proposal.

Dr. Kemp stated that he hoped Auburn would document, in writing, the information presented to the Committee orally. He then moved that the Committee approve the proposal with the following conditions:

A) that the experiments be limited to two years with the possibility of an extension for up to one year by ABRAC, contingent on submission of a progress report submitted at the end of the initial two years;

B) that the minimum size of the fry introduced into the outdoor ponds will be no smaller than 0.5 cm long;

C) that there will be no release of fry into the ponds during the winter months when flooding is more likely to occur due to the rainy season;

D) that the number of transgenic fish in each test pond will be reduced to no more than 300 during the winter months and,

E) that the PI identify on the map of the facility provided to ABRAC, the 10 test ponds designated for the experiment in order to document that the ponds fit the oral description given i.e., that no more than 10 percent of the perimeter of the designated ponds have narrower (4 foot) levees and that these are flanked by adjacent ponds outside the fence.

The motion was seconded.

Dr. Korwek asked why two years should elapse before an interim report? Dr. Kemp replied that because it would take two years before significant data could be collected.

Dr. Dunham said that it would take 2 years to complete the proposed experiments if progeny could be produced this spring, otherwise it would take longer. Dr. Frey said the report should be required two years from the fertilization date, not two years from the date of the ABRAC meeting. Dr. Kemp said he meant two years from the start of the experiment.

Dr. Gould questioned the impact of requiring the fry to be at least 0.5 cm before they are introduced into the ponds. Dr. Dunham replied that it would limit the number of fish used and lengthen the experiment because it takes 3 months for the fry to reach that size indoors, while outdoors it takes only 14-21 days. The numbers of fish would have to be reduced from 50,000 to 5-10,000.

Dr. Hill asked Dr. Kemp to clarify how an extension would be granted at the end of two years. Dr. Kemp said ABRAC would have to review the experiment again and decide if an extension should be granted.
Dr. Whitmore said that he had some serious concerns about the proposal and therefore was going to vote against the motion unless new information was presented. He said he was concerned about ambiguity over whether certain stages of the experiments had already been done in the laboratory or not. He said that a statement should be included in the minutes saying that the Committee was basing its decision on the presumption that the work had been done indoors.

Dr. Tolin disagreed noting that not every step in an experiment needs to be done indoors first. Sometimes it may not be appropriate to work indoors, say for example in tree research. Dr. Whitmore said he didn't mean every step needed to be done indoors, but those which could be done indoors, should be.

Ms. Hollander reiterated her opinion that the Committee should have more data. However, she said she was very sympathetic to Auburn's situation and concerned that the fish could not be kept alive indefinitely while data were supplied. She asked if the Committee might give approval for the six adult fish to be released into the ponds now, and then Auburn could submit additional data and the ABRAC could vote on the rest of the proposal at its June meeting.

Dr. Bothast asked if Ms. Hollander was recommending this on the basis of considering the experimental ponds a contained facility for the larger fish? He said he had some doubts about considering these as containment. Ms. Hollander said she did not want to say that this was containment. Dr. Tolin said she thought that the experimental ponds would meet the standards of containment (for large fish) defined in Appendix Q of the NIH-RAC Guidelines. Dr. Kemp said if this is the case, then the proposal was at a confinement level of high four and therefore the Committee should be able to reach a decision at the current meeting. Dr. Frey agreed that the confinement level justified proceeding at once.

Dr. Sorenson asked about documentation. She said she would like to see the data from the Israeli experiments and the others described. Dr. Tolin said she felt more comfortable voting in favor of the proposal now that she had heard the information presented orally to the Committee.

Dr. Gould said he would like to see documentation and a description of the potential benefits of the experiment. Dr. Kemp said the ABRAC needed to discuss providing information on benefits as part of their procedures, but that he didn't want to include this requirement in his current motion. Dr. Gould agreed to defer it for now, but he said in the future this information should be required. He also said that he was concerned that not requiring such data this time might set a precedent. Dr. Osburn stated that considering benefits was not part of the charge of the ABRAC. Dr. Young clarified that the decision of ABRAC is a recommendation to the Assistant Secretary, Dr. Bentley, and that Dr. Bentley would weigh it and other factors before making a decision. ABRAC is an advisory panel.

Dr. Vidaver said the Committee had received a great deal of information orally and suggested that it would be prudent to put some of this information in the Federal Register for public comment. Ms. Cordle said the experiments will require an environmental assessment (EA) and that this process will involve public comment. Dr. Tolin said that there could be a separate meeting to announce the EA and that a file of written documentation could be made available for public scrutiny at such a meeting.
Dr. Gould offered an amendment that the fry not be released into the ponds until they reached 1 gram weight. Dr. Kemp declined to accept this amendment to his motion.

Ms. Hollander asked if Dr. Kemp's motion was conditional on receipt of written documentation supporting the information given orally to the Committee? Dr. Kemp said that it was not.

The Committee voted on Dr. Kemp's motion concerning the Auburn proposal and it was passed, 7 in favor and 6 opposed.

Dr. Young commented that a 7 to 6 vote did not reflect a clear mandate for approval.

Dr. Frey asked the six members who voted against the motion for their reasons. He asked if their objections were procedural or scientific?

Dr. Gould said he had voted against the motion because he believed it should be contingent on receiving and reviewing additional data. He said he believed the information provided orally should be documented in writing.

Dr. Tolin asked about timing. She asked Dr. Dunham if the big fish were introduced into the ponds now, how long it would be before the fingerlings were large enough to be put outdoors? Dr. Dunham responded that if the fish were put into the ponds immediately, they would spawn about May 1, and thus it would be about June 1 before the fry would reach 0.5 cm. Dr. Tolin noted that the ABRAC would meet again on June 22, thus the Committee might consider giving conditional approval for release of the large fish into the ponds now,

and defer formal approval until the next meeting, leaving the time for additional data to be reviewed.

Dr. Kemp noted that the Committee had already voted to approve the proposal. Dr. Frey agreed, saying he objected to the ABRAC trying to manage research rather than just reviewing proposals for possible adverse effects.

Dr. Hill said he sympathized with those members who believed that more written documentation was necessary. Unfortunately, he said the PI hadn't been asked to provide this documentation earlier. He said the Committee should request the information in a timely manner and move ahead.

Dr. Kemp said he would be willing to modify his original motion to be contingent on providing written documentation which supports the information given orally to the Committee.

Dr. Korwek asked who would make the determination if the material provided was sufficient? Dr. Whitmore replied that the Committee had already approved the proposal and that OAB staff could determine if the written documentation was sufficient. He said he could not change his vote until he was assured that documentation which confirmed the information given orally had been provided.

Dr. Hollinshead said she was puzzled by the Committee's willingness to require something like a full grant proposal. She said if additional information were to be required from the PI's, this should be stated up front in a form.

Drs. Tolin and Sorenson said they were satisfied with the biosafety of the proposal, but they were not satisfied with the precedent of approving without written documentation. Dr. Tolin said she would like to see more on standard practices for fish and the molecular biology of the experiments.

Dr. Korwek said he wanted to see the experiments go forward and that the Committee had already given conditional approval. However, the heart of the matter was that the written documentation presented was inadequate. He said that additional information should be requested, but that someone should read it and make a decision.

Dr. Kemp asked if Dr. Korwek would be comfortable if a subcommittee were appointed to review the material? Dr. Korwek said that he would. Dr. Korwek then moved that a subcommittee be formed to review documentation to ensure that it was adequate and complete. The motion was seconded.

Ms. Hollander asked what Auburn was supposed to do in the meantime? Did they have to wait or could the large fish be placed in the outdoor ponds before the additional documentation was reviewed?

Dr. Gould stated that this was a precedent setting case. He said he would prefer that a fisheries expert be included on the subcommittee. Ms. Hollander concurred. Dr. Korwek replied that he would accept requiring a fish expert to serve on the subcommittee, as part of his motion, but only if this did not involve re-reviewing the proposal.

Dr. Frobish said that Auburn University would work with OAB to get the information required by mid-April. However, he requested that the experiments not be held up unduly or another year might be lost.

Dr. Langston suggested that more confinement procedures be added, i.e., that the ponds be drained at the end of the experiments into a common pond. Dr. Korwek replied that the Committee was generally satisfied with the biosafety provisions and that the issue that remained was documentation. Dr. Witter noted that the subcommittee should provide Auburn with a list of the documentation required.

Dr. Margaret Mellon, NWF, stated that the Committee should proceed cautiously. She said it was not only necessary for the Committee to satisfy itself technically with the decision, but it should also consider how an impartial judge would react to reading the meeting transcript. She said this was particularly important with regard to the subcommittee because their deliberations might not be open for public participation. She added that OAB might wish to consult a USDA lawyer on this point.

The Committee then voted on Dr. Korwek's motion to form a subcommittee to evaluate the Auburn documentation. It was passed, 10 in favor, 0 opposed and 2 abstaining.

Dr. Osburn then asked for volunteers to serve on the subcommittee. Drs. Tolin, Witter, and Gould volunteered. Dr. Young said the complete record of the subcommittee would be provided to Dr. Bentley for his consideration.

Ms. Hollander moved that ABRAC co-sponsor with other organizations a conference to explore the ecological, economic and social implications of transgenic fish research. Dr. MacKenzie said a recent conference had dealt with these issues, at least in part. Ms. Hollander said fish issues were especially vexing and required special action. Dr. Sorenson agreed.

Dr. Chen commented that researchers need guidelines for fish experiments and biotechnology in general, not just transgenic fish. He urged the Federal government to work out a successful set of guidelines. He added that field investigators need this guidance to compete in the international transgenic animal arena.

Dr. Hollinshead said that insufficient data exists for such a meeting on transgenic fish.

The Committee voted on Ms. Hollander's motion to cosponsor a conference on transgenic fish and it was passed, 8 in favor, 1 against, and 3 abstentions.

Dr. Frobish asked what specific information was now required of Auburn University. Dr. Osburn said a list would be provided in a timely fashion by OAB.

Dr. Kemp then moved that his original motion be reconsidered, with the inclusion of making it contingent on the formation and approval of the

subcommittee, which will verify the accuracy of supporting data provided by Auburn. The motion was seconded.

Ms. Cordle said that the Assistant Secretary cannot approve the proposal until the EA is completed. Dr. Young added that this would be 30 days minimum, and that OAB would go forward with the EA at this point.

Dr. Gould asked for clarification on whether the large fish could be released into the large ponds in the interim. Dr. Young said it was his understanding that they could be.

Dr. Kemp's reformulated motion conditioning ABRAC approval of the Auburn proposal on subcommittee review and approval was voted upon and passed, 9 in favor, 2 opposed, and 2 abstaining.

Travel Information

Dr. Young introduced Mr. Barry Stone of OAB, who is responsible for the travel documentation for ABRAC meetings. Mr. Stone said that the official USDA servicing travel agency was Heritage Travel. He added that Heritage could arrange airline reservations for the ABRAC members, guarantee the government rate, and the tickets could be charged to the Office of the Secretary's Diners Club account making it more convenient and practical for the traveler. Mr. Stone distributed a profile form for each member to fill out voluntarily and return in the postage-paid envelope attached and said he could be contacted at (202) 475-5723 for any questions. He also said that a pre-paid ticket could be sent to the traveler if desired. He also noted that airline penalty fees for cancellation are not normally reimbursed by USDA.

The Handbook

Dr. Osburn asked the Committee for comments on the revised Handbook.

Dr. Frey commented on the broad definition of biotechnology in the Handbook.

Dr. Korwek said the regulatory section was sometimes misleading. He said that the authors should avoid making blanket statements.

Dr. Gould said he believed the sections on public relations and social implications should stay in. However, he said the tone was still not correct. He recommended bringing in an outside expert who is an expert in these matters.

Dr. Kemp said the requirements for the PI should be addressed either in the Handbook or the Guidelines.

USDA Guidelines for Research Outside the Laboratory

Dr. Osburn asked the Committee to return their attention to the Guidelines.

Mr. Stern then asked the Committee to comment on Section IX, particularly with regard to the criteria for public members. Ms Hollander responded that the

Guidelines need to ensure the interest of the community and the language should reflect this and that perhaps the Guidelines should include the reference to representatives of non-governmental organizations.

Mr. Stern said he believed it was the sense of the Committee not to include details such as notifying newspapers of IBC meetings, etc., but perhaps a provision should be added stating that if 10 people petitioned, then an IBC meeting should be opened to the public. Ms. Hollander said such a provision should be added and that the Guidelines should stress involving the public making decisions.

Ms. Hollander asked why a requirement for public meetings would be difficult to meet? She said the she believed that IBC's should hold some public meetings. Dr. Osburn replied that announcing weekly meetings would be burdensome. Dr. Young said USDA did not have the authority to require that IBC meetings be open to the public. Dr. Korwek disagreed saying that the Guidelines could specify compliance in such matters. Dr. MacKenzie noted that open meetings would be difficult, practically speaking, because a great deal of IBC business is handled by mail. Dr. Purchase remarked that there is a difference between an "open" meeting and a "public" meeting.

Dr. Gould commented on Section X-B regarding composition of the IBC's. He said this section did not grant ABRAC much authority to review IBC's. Dr. Tolin said the RAC did not review IBC's. Dr. Kemp suggested that the Guidelines state that ABRAC reserves the right to review the composition of IBC's. Ms. Hollander agreed. Dr. Osburn said OAB should redraft this section using the suggestions of the Committee.

Dr. Kemp asked for clarification of Section X-B-2 regarding conflict of interest. He said the did not understand how "direct financial interest" is defined. Ms. Hollander said it should be defined in the Guidelines. Mr. Stern noted that conflict of interest provisions would affect private companies differently than they would affect government or university bodies. Dr. Vidaver noted that there are other types of conflict of interest than financial. Dr. Osburn said that in the interest of time the Committee members should send OAB their comments on this section right away so that they could be considered.

Dr. Young said that OAB wanted the Committee's permission to go to the Biotechnology Science Coordinating Committee, Office of Management and Budget and then proceed to the Federal Register in June with both the Handbook and the Guidelines. This was moved and seconded. It was passed 10 in favor, 0 opposed, and 0 abstaining.

Dr. Hollinshead called the Committee's attention to Section X-B-2-b. She said that this could be amended to read "in which he or she has a direct conflict of interest..." She also noted that Section X-B-2-c was also very unclear.

Mr. Stern asked for the Committee's comments on definitions. Ms Hollander said it was convenient to have the definitions listed in one place. Dr. Kemp said this section could be addressed after public comment. Dr. Korwek said

definitions are useful, but not every term needs to be defined, so OAB should aim for a happy medium.

Dr. Gould asked that the preamble should go to ABRAC for comment before it goes to the public. Dr. Young said that it will.

Dr. Tolin said she will work on Section IV, regarding data requirements for the PI. She will recommend that this include three areas: classifying the unmodified organisms; classifying the type of modification; and describing the appropriate confinement procedures. Dr. Hollinshead suggested that this should be done in chart form.

The meeting was adjourned at 3:45 p.m., March 23, 1989.

Martha B. Steinbock
Rapporteur

Alvin L. Young
Executive Secretary

Bonnie I. Osburn
Chair

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